

### **REMARKS**

Claims 94-96 and 98-116 are pending in this application. Also, claims 1-93 were previously cancelled and claims 97 has been cancelled at this time. Further, claims 96, 101 and 106-116 have been withdrawn. Furthermore, claims 94 and 102 have been amended, which amendments find support at least at page 75, lines 33-34 and the Examples of the present specification, respectively.

In light of remarks set forth below, reconsideration and withdrawal of all outstanding rejections are respectfully requested.

### **Election/Restriction**

The Examiner states that arguments regarding Tibor Mora (USP 2,719,179) and Shah et al. (WO 98/41545) are not persuasive.

Concerning Tibor Mora, column 3, lines 16-19 and column 7, lines 44-45 and 64-70, cited by the Examiner, it is noted that these passages do not indicate reactions of two different molecular species, but can be interpreted as reactions of single molecular species with multiple alternatives.

Nevertheless, since the Examiner has made Election/Restriction Requirement final, claims 96, 101, and 106-116 have been withdrawn from further consideration without canceling these non-elected claims. However, at least due to being dependent upon claim 94, Applicants respectfully request examination and allowance of certain withdrawn claims, especially claims 96, 101 and 106-111.

### **Claim Objections**

The Examiner has objected to claims 97 and 102.

To address these objections, claim 97 has been cancelled to avoid duplication of claim 94, and claim 102 has been amended as explained below. By way of this submission, the objections to claims 97 and 102 are rendered moot.

### **Issues under 35 USC § 112**

The Examiner has rejected claim 102 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Also, the Examiner has also rejected claim 102 under 35 U.S.C. § 112, second paragraph, stating that the term “minimum” in claim 102 is a relative term which renders the claim indefinite because written description is not disclosed as to what minimum amounts of anhydro products are.

These rejections are respectfully traversed.

On page 7 of the outstanding Office Action, the Examiner indicates that applicants fail to provide information sufficient to practice the claimed invention for all possible reactions wherein the reaction products do not contain minimum amounts of anhydro products or contain minimum amounts of **anhydro** products.

The Examiner interprets the term “anhydro” to mean cyclized forms of monosaccharides, such as glucopyranose. The present specification, however, describes synthesis of glycoconjugates of monosaccharides such as oligosaccharides or polysaccharides. The oligosaccharides or polysaccharides contain monosaccharide residues which are already in ring form, such as pyranose or furanose. Therefore it is evident that the anhydroform of the present

invention means additional water cleavage products of the saccharides formed. Further the present invention clearly proves such production by way of mass spectrometry showing that such water cleavage products are formed.

In particular, according to the present specification, the term “anhydro products” refers to dehydrated products and levoglucosan, see page 53, lines 28-37; and page 41, lines 14-16 of the present specification.

Further, it is shown in the beginning of Example 1 that the dehydrated products are smaller than 18 Da products. These products are also clearly visible in the Figures as dehydrated products. For example, see, e.g, page 89, lines 8-9, page 89, lines 11-16; page 89, lines 34-35; page 89, lines 24-26; and page 90, lines 16-17 and Figures disclosed therein of the present specification.

Though the exact molecular structures are not shown for the anhydro products, a skilled artisan can monitor the cleavage products by mass spectrometry. Since the current methods do not involve complex chemical synthesis but simple incubations with catalysts, it is easily possible for a skilled artisan to analyze and control the anhydro side products.

On page 8 of the outstanding Office Action as noted by the Examiner, the present specification does not contain any direct definition of the term “minimal” in the claim. However, it is disclosed that too high amounts of anhydro products cause bitter taste or undesired color. Illustrative reference is made to page 4, lines 32-34.

Therefore, amended claim 102 recites that the reaction products do not contain anhydro products or contain an amount of anhydroproducts, which do not cause bitter taste or undesired

color to the reaction products, wherein said anhydro products are levoglucosan and/or dehydrated products.

By way of this submission, 35 USC 112 rejections have been overcome. Accordingly, reconsideration and withdrawal of these rejections are respectfully requested.

**Issues under 35 U.S.C. §§ 102(b)/103(a)**

The Examiner has rejected claims 94, 95, 97, 98, 100, 103, and 104 under 35 U.S.C. § 102 (b) as being anticipated by Hindsgaul et al. (WO 96/06102, hereinafter Hindsgaul '102). Also, the Examiner has rejected claims 94 and 99 under 35 U.S.C. § 103(a) as being obvious over Hindsgaul '102 in view of Rennhard (USP No. 3,766,165).

These rejections are respectfully requested.

While not conceding to the Examiner's rejections, claim 94 has been amended to further emphasize the distinctions between the present invention and the cited art. By way of this submission, the prior art rejections are moot. However, Applicants provide more detailed discussions as set forth below.

**The Present Invention and Its Advantages**

The present invention of claim 94 is directed to a method for the preparation of glycoconjugates comprising reacting under condensing conditions involving acid or metal catalysis at least two non-protected saccharides selected from the group consisting of: A. aldomonosaccharides, B. deoxyhexoses, C. N-acetyldoses, D. sialic acids, E. hexuronic acids, H. oligosaccharides containing a saccharide from any one of groups A – E, G.

polysaccharides containing a saccharide from any one of groups A – E, so that said saccharides are selected from at least two of groups A – G; in order to form a glycosidic bond between said saccharides through any free hydroxyl group position in said saccharides, wherein C1-positions of the reacting saccharides are not protected. The present invention is mainly directed to the use of non-protected carbohydrates, such as monosaccharides, oligosaccharides and polysaccharides. The use of non-protected carbohydrates makes the process much more cost-effective and gives high variability in the carbohydrate libraries to be produced.

#### The Distinctions between the Present Invention and the Cited Art

Hindsgaul '102 method involves substitution of a "core" oligosaccharide by identical substituents. As a result, the size of the oligosaccharide product varies only by the number of identical branches on the core part.

In contrast to what is considered by the Examiner, Applicants respectfully submit that Hindsgaul '102 does not disclose or suggest the use of non-protected monosaccharides. In the reactions of Hindsgaul '102, there is one derivatized component, which is protected (or activated at position 1). The C1 alkyl ester (page 4, lines 8-9) referred by the Examiner is position 1 or glycosidic derivative of N-acetylglucosamine, not "a N-acetylglucosamine", which is "a reducing monosaccharide" according to the IUPAC definition. The glycoside of monosaccharide is referred as the core structure, i.e., item (2) of claim 1 of Hindsgaul '102.

Also, the cited position of GlcNAc (see page 4, lines 8-9 of the Hindsgaul '102) indicates an N-acylglucosamine. However, page 4, lines 1-2 of Hindsgaul '102 discloses that the meaning

of this is to combine the glycosides as sugar monomers with substitutions, which are listed on page 4, lines 9-15 of Hindsgaul '102.

On the other hand, the present invention is particularly directed to totally non-protected monosaccharides. For example, a reference is made to the following parts of the present specification:

page 75, lines 33-34:

*"When the general methods according to the invention are used the C1-position of the saccharides are not protected"*

page 16, lines 33-35, showing that the term "reducing" means also that C1 is not substituted:

*"The method of the invention comprises producing a saccharide or glycoconjugate from a free non-protected reducing monosaccharide involving condensation polymerisation or oligomerization of a monosaccharide"*

page 63, lines 2-9:

*"The present invention is in specific embodiment directed to the novel method to produce non-reducing monosaccharides, and/or oligosaccharides and/or polysaccharides using acid catalysis according to the Scheme 3: SAC+polyol->SAC-polyol wherein SAC is a non-protected reducing monosaccharide, oligosaccharide or polysaccharide or mixtures thereof"*

page 48, lines 34-36:

*"The invention provides a method to produce a saccharide or glycoconjugate from free non-protected reducing monosaccharide or oligosaccharide involving acid catalysed polymerisation or oligomerization of a monosaccharide"*

page 22, lines 12-14:

*"The term non-protected means that the residues have not been modified by protecting groups used in carbohydrate chemistry."*

It is further noted that the reactions of Hindsgaul '102 use activated donor monosaccharide glycosides, which are not non-protected as in the present invention, e.g. Gal-

imidate (See, page 13 of Hindsgaul '102). It means that Hindsgaul '102 considers only non-anomeric hydroxyls as positions for protection, when actually the core structure of Hindsgaul '102 is also a protecting group. The complex chemical process of Hindsgaul '102 involving the core structure and activated monosaccharide donors is clearly chemically different from the method of the present invention, giving different products.

It is further realized that the products of the present invention are distinguishable from that of the Hindsgaul '102 including the reducing end derivatized residue.

Therefore, the present invention is neither anticipated by nor obvious over Hindsgaul '102.

Regarding Hindsgaul '102 in view of Rennhard, the second reference Rennhard cannot make up for the deficiencies of the primary reference Hands Gaul '102. Specifically, as it is discussed above, Hindsgaul '102 fails to disclose or suggest the method of the claimed invention related to condensation of at least two non-protected saccharides. Therefore, it is clear that the combination of Hindsgaul '102 and Rennhard cannot arrive at the present invention. Rennhard is directed to the use of polyols and does not add anything to the teachings of Hindsgaul '102 with regard to the use of non-protected saccharides. Since the cited art fails to disclose or suggest the condensation of at least two non-protected saccharides, the present invention is patentably distinct from the combined teaching of the cited art.

In view of the above remarks, Applicants submit that the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie Reg. No.

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42,874 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.147; particularly, extension of time fees.

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Respectfully submitted,

By 

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